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IFee

November 3, 2004

Mail Stop Amendment
Commissioner for Patents
Post Office Box 1450
Alexandria, VA 22313-1450

Re: U.S. Patent Application No. 10/718,765
For: *Use Of Creatine Or Creatine Analogs for the Treatment
of Diseases of the Nervous System*
Inventors: Kaddurah-Daouk, Rima *et al.*
Filed: November 21, 2003
Our Ref. No.: AVZ-001CPUSCN2

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form SB/08;
3. Copy of the publication cited in PTO Form SB/08 (1); and
4. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. *For this purpose, a duplicate of this sheet is attached.*

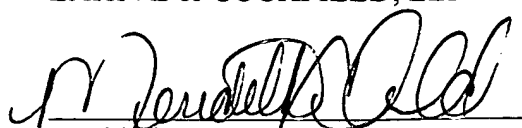
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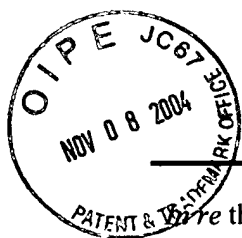
November 3, 2004

Date

Merideth C. Arnold, Registration No. 52,568

Respectfully submitted,
LAHIVE & COCKFIELD, LLP


Merideth C. Arnold, Esq.
Registration No. 52,568
Attorney for Applicants



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re the application of: Kaddurah-Daouk, Rima, *et al.*

Serial No.: 10/718,765

Filed: November 21, 2003

For: *Use of Creatine or Creatine Analogs for the
Treatment of Diseases of the Nervous System*

Attorney Docket No.: AVZ-001CPUSCN2

Group Art Unit: 1639

Examiner: Not Yet Assigned

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Commissioner for Patents
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Certificate of First Class Mailing (37 CFR §1.8(a))

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November 3, 2004

Date of Signature and of Mail Deposit

By:

Merideth C. Arnold, Esq.
Registration No. 52,568
Attorney for Applicants

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

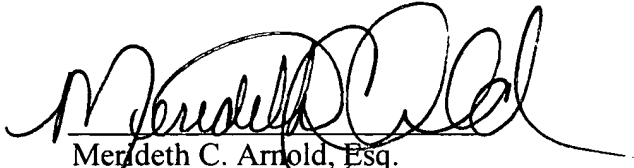
For the Examiner's convenience in reviewing this continuation application, Applicants submit a consolidated PTO Form SB/08, listing all references cited during the prosecution of the parent application. References A1-A4, A6-A14, and B1-H2 were previously cited and submitted to the Office in U.S. Application Serial No. 08/853,174, filed May 7, 1997 (Atty. Docket No. AVZ-001CPUS), of which this application is a continuation and to which this application claims priority. In accordance with 37 CFR §1.98(d), these references are not enclosed herewith, but will be provided upon request. In addition, this Information Disclosure

Statement presents reference A5, not previously submitted to the Office, which is enclosed herewith in accordance with 37 CFR §1.97.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

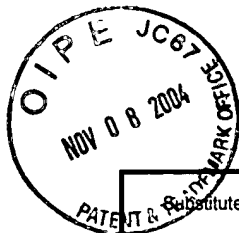


Meredith C. Arnold, Esq.
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Attorney for Applicants

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Boston, MA 02109
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Date: **November 3, 2004**

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PTO/SB/08a/b (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	10/718,765
				Filing Date	November 21, 2003
				First Named Inventor	Kaddurah-Daouk, Rima
				Art Unit	1639
				Examiner Name	Not Yet Assigned
Sheet	1	of	8	Attorney Docket Number	AVZ-001CPUSCN2

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	A1	5,091,404	02-25-1992	Elgebaly, S.A.	
	A2	5,321,030	06-14-1994	Kaddurah-Daouk, R., <i>et al.</i>	
	A3	5,324,731	06-28-1994	Kaddurah-Daouk, R., <i>et al.</i>	
	A4	5,492,930	02-20-1996	Coffin, V.L.	
	A5	5,676,976	10-14-1997	Teicher, B.A., <i>et al.</i>	
	A6	5,741,661	04-21-1998	Goldin, S.M., <i>et al.</i>	
	A7	6,169,115	01-02-2001	Kaddurah-Daouk, R., <i>et al.</i>	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ³
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	A8	WO 90/09192	08-23-1990	Massachusetts Institute of Technology (US)		
	A9	WO 92/08456	05-29-1992	Amira Inc. (US)		
	A10	WO 94/16687	08-04-1994	University of Pennsylvania (US)		
	A11	WO 94/17794 A1	08-18-1994	Jennings, S.A. (GB)		

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	A12	Annesley, T., <i>et al.</i> , "Cyclocreatine Phosphate as a Substitute for Creatine Phosphate in Vertebrate Tissue. Energetic Considerations," <i>Biochem. Biophys. Res. Commun.</i> , 1977; 74:185-90.	
	A13	Annesley, T., <i>et al.</i> , "Formation and Utilization of Novel High Energy Phosphate Reservoirs in Ehrlich Ascites Tumor Cells," <i>J. Biol. Chem.</i> , 1978; 253(22):8120-5.	
	A14	Beal, M., "Aging, Energy, and Oxidative Stress in Neurodegenerative Diseases," <i>Ann. Neurol.</i> , 1995; 38:357-66.	

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	B1	Beal, M., "Does Impairment of Energy Metabolism Result in Excitotoxic Neuronal Death in Neurodegenerative Illnesses?" <i>Ann. Neurol.</i> , 1992; 31:119-30.	
	B2	Beal, M. <i>et al.</i> , "Age-Dependent Striatal Excitotoxic Lesions Produced by the Endogenous Mitochondrial Inhibitor Malonate," <i>J. Neurochem.</i> , 1993; 61:1147-50.	
	B3	Bertolini, <i>et al.</i> , Chemical Abstracts AN 1982:49622.	
	B4	Brady, S., <i>et al.</i> , "Nerve-Specific Enolase and Creatine Phosphokinase in Axonal Transport: Soluble Proteins and the Axoplasmic Matrix," <i>Cell</i> , 1981; 23:515-23.	
	B5	Brouillet, E., <i>et al.</i> , "Chronic Mitochondrial Energy Impairment Produces Selective Striatal Degeneration and Abnormal Choreiform Movements in Primates," <i>PNAS</i> , 1995; 92:7105-9.	
	B6	Browne, S., <i>et al.</i> , "Oxidative Damage and Metabolic Dysfunction in Huntington's Disease: Selective Vulnerability of the Basal Ganglia," <i>Ann. Neurol.</i> , 1997; 41:646-53.	
	B7	Burbaeva, G.S., <i>et al.</i> , "Decreased Level of Immunoreactive Phosphokinase BB Isoenzymes in the Brain of Patients with Schizophrenia and Senile Dementia of the Alzheimer Type," <i>Zh. Nevropatol. Psikiatr Im S S Korsakova</i> , 1990; 90(7):85-7.	
	B8	Cadoux-Hudson, T., <i>et al.</i> , "Imaging of Human Brain Creatine Kinase Activity in Vivo," <i>FASEB J.</i> , 1989; 3:2660-6.	

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				First Named Inventor	Kaddurah-Daouk, Rima
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Sheet	3	of	8	Attorney Docket Number	AVZ-001CPUSCN2

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FOREIGN PATENT DOCUMENTS						
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	C1	Carter, A.J., <i>et al.</i> , "Preincubation with creatine enhances levels of creatine phosphate and prevents anoxic damage in rat hippocampal slices," <i>J Neurochem.</i> 1995; 64(6):2691-9.		
	C2	Chandler, W., <i>et al.</i> , "Regional Creatine Kinase, Adenylate Kinase, and Lactate Dehydrogenase in Normal Canine Brain," <i>Stroke</i> , 1988; 19:251-5.		
	C3	Cramer, F., <i>et al.</i> , "Die Synthese der Argininphosphorsäure und die Reaktion von Isoeuidophosphonaten mit Amininen," <i>Chem. Ber.</i> , 1962; 95:1670-82.		
	C4	De Leon, M., <i>et al.</i> , "Identification of Transcriptionally Regulated Genes After Sciatic Nerve Injury," <i>J. Neurosci. Res.</i> , 1991; 29:437-48.		
	C5	Erecinska, M., <i>et al.</i> , "ATP and Brain Function," <i>J. Cerebr. Bloof Flow and Metabolism</i> , 1989; 9:2-19.		
	C6	Friedhoff, A., <i>et al.</i> , "Creatine Kinase Isoenzyme Associated with Synaptosomal Membrane and Synaptic Vesicles," <i>Life Sci.</i> , 1977; 20:867-74.		
	C7	Goodman & Gilman, <i>The Pharmacological Basis of Therapeutics</i> , 1980, 6 th Ed. (MacMillan Pub.); 5-10.		
	C8	Griffiths, G., <i>et al.</i> , "Accumulation of Analog of Phosphocreatine in Muscle of Chicks Fed 1-Carboxymethyl-2-iminoimidazolidine (Cyclocreatine)," <i>J. Biol. Chem.</i> , 1976; 251(7):2049-54.		

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Sheet	4	of	8	Attorney Docket Number	AVZ-001CPUSCN2

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	D1	Gu, M., <i>et al.</i> , "Mitochondrial Defect in Huntington's Disease Caudate Nucleus," <i>Ann. Neurol.</i> , 1996; 39:385-9.		
	D2	Gurney, M., <i>et al.</i> , "Motor Neuron Degeneration in Mice That Express a Human Cu,Zn Superoxide Dismutase Mutation," <i>Science</i> , 1994; 264:1772-5.		
	D3	Hemmer, W., <i>et al.</i> , "Functional Aspects of Creatine Kinase in Brain," <i>Dev. Neuroscience</i> , 1993; 15:249-260.		
	D4	Hagenfeldt, L., <i>et al.</i> , "Creatine Treatment in MELAS," <i>Muscle and Nerve</i> , 1994; 10:1236-7.		
	D5	Hemmer, W., <i>et al.</i> , "Creatine Kinase Isoenzymes in Chicken Cerebellum: Specific Localization of Brain-type Creatine Kinase in Bergmann Glial Cells and Muscle-type Creatine Kinase in Purkinje Neurons," <i>Eur. J. Neuroscience</i> , 1994; 6:538-49.		
	D6	Henshaw, R., <i>et al.</i> , "Malonate Produces Striatal Lesions by Indirect NMDA Receptor Activation," <i>Brain Research</i> , 1994; 647:161-6.		
	D7	Hertz, L., <i>et al.</i> , "Energy Metabolism at the Cellular Level of the CNS," <i>Can. J. Physiol. Pharmacol.</i> , 1992; 70:S145-57.		
	D8	Ito, M., "The Cellular Basis of Cerebellar Plasticity," <i>Corr. Opin. Neurobiol.</i> , 1991; 1:616-20.		
	D9	Jenkins, B., <i>et al.</i> , "Evidence for Impairment of Energy Metabolism in Vivo in Huntington's Disease Using Localized 1H NMR Spectroscopy," <i>Neurology</i> , 1993; 43:2689-95.		

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	E1	Kahn, M.A., "Effect of Calcium on Creatine Kinase Activity of Cerebellum," <i>Histochem.</i> , 1976; 48:29-32.		
	E2	Lillie, J., <i>et al.</i> , "Cyclocreatine (1-Carboxymethyl-2-iminoimidazolidine) Inhibits Growth of a Broad Spectrum of Cancer Cells Derived from Solid Tumors," <i>Cancer Res.</i> , 1993; 53:3172-8.		
	E3	Lim, L., <i>et al.</i> , "Neurone-Specific Enolase and Creatine Phosphokinase are Protein Components of Rat Brain Synaptic Plasma Membranes," <i>J. Neurochem.</i> , 1983; 41:1177-82.		
	E4	LoPresti, P., <i>et al.</i> , "Direct Determination of Creatine Kinase Equilibrium Constants with Creatine or Cyclocreatine as Substrate," <i>Biochem. Biophys. Acta.</i> , 1989; 998:317-20.		
	E5	Lowe, G., <i>et al.</i> , "Evidence for an Associative Mechanism in the Phosphoryl Transfer Step Catalyzed by Rabbit Muscle Creatine Kinase," <i>J. Biol. Chem.</i> , 1980; 225(9):3944-51.		
	E6	Maker, H., <i>et al.</i> , "Regional Changes in Cerebellar Creatine Phosphate Metabolism During Late Maturation," <i>Exp. Neurol.</i> , 1973; 38:295-300.		
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	E9	McLaughlin, A., <i>et al.</i> , "Specificity of Creatine Kinase for Guanidino Substrates," <i>J. Biol. Chem.</i> , 1972; 247(13):4382-8.		

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				Application Number	10/718,765
				Filing Date	November 21, 2003
				First Named Inventor	Kaddurah-Daouk, Rima
				Art Unit	1639
				Examiner Name	Not Yet Assigned
Sheet	6	of	8	Attorney Docket Number	AVZ-001CPUSCN2

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	F1	Molloy, G., <i>et al.</i> , "Rat Brain Creatine Kinase Messenger RNA Levels are High in Primary Cultures of Brain Astrocytes and Oligodendrocytes and Low in Neurons," <i>J. Neurochem.</i> , 1992; 59:1925-32.	
	F2	National Library of Medicine: IGM Metathesaurus Information Screen - Nervous System Diseases definitions and related terms.	
	F3	Newman, E., "Regulation of Potassium Levels by Glial Cells in the Retina," <i>Trends Neuroscience</i> , 1985; 8:156-9.	
	F4	Oblinger, M., <i>et al.</i> , "Cytotypic Differences in the Protein Composition of the Axonally Transported Cytoskeleton in Mammalian Neurons," <i>J. Neurol.</i> , 1987; 7(2):453-62.	
	F5	Orlovskaja, D.D., <i>et al.</i> , "Neuromorphology and Neurochemistry of Senile Dementias in the Light of Studies on Glial Response," <i>Vestn Ross Akad Med Nauk.</i> , 1992; 8:34-9.	
	F6	Rees, <i>et al.</i> , Chemical Abstracts AN 89:82648, US patent 4,981,774.	
	F7	Reichenbach, A., "Glial K ⁺ Permeability and CNS K ⁺ Clearance by Diffusion and Spatial Buffering," <i>Acad. Sci. New York</i> , 1991; 272-86.	
	F8	Roberts, J., <i>et al.</i> , "Higher Homolog and N-Ethyl Analog of Creatine as Synthetic Phosphagen Precursors in Brain, Heart, and Muscle, Repressors of Liver Amidinotransferase, and Substrates for Creatine Catabolic Enzymes," <i>J. Biol. Chem.</i> , 1985; 260(25):13502-8.	

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	G1	Roberts, J., <i>et al.</i> , "Synthesis and Accumulation of an Extremely Stable High-Energy Phosphate Compound by Muscle, Heart, and Brain of Animals Fed the Creatine Analog, 1-Carboxyethyl-2-iminoimidazolidine (Homocyclocreatine)," <i>Arch. Biochem. Biophys.</i> , 1983; 220(2):563-71.			
	G2	Rowley, G.L., <i>et al.</i> , "On the Specificity of Creatine Kinase. New Glycocyamines and Glycocyamine Analogs Related to Creatine," <i>Journal of the American Chemical Society</i> , 1971; 93:5542-51.			
	G3	Rudinger, "Peptide Hormones," 1976 (J. Parsons Ed.); 1-6.			
	G4	Schiffmann, R., <i>et al.</i> , "Childhood Ataxia with Diffuse Central Nervous System Hypomyelination," <i>Ann. Neurol.</i> , 1994; 35:331-40.			
	G5	Schulthesis, <i>et al.</i> , "Effects of Creatine on Synthesis and Release of Gamma-[3H] Aminobutyric Acid," <i>Journal of Neurochemistry</i> , 54(6):1858-63.			
	G6	Schultz, J., <i>et al.</i> , "Blockade of Neuronal Nitric Oxide Synthase Protects Against Excitotoxicity in vivo," <i>J. Neurosci.</i> , 1995; 15(12):8419-29.			
	G7	Schultz, J., <i>et al.</i> , "Inhibition of Neuronal Nitric Oxide Synthase by 7-Nitroindazole Protects Against MPTP-Induced Neurotoxicity in Mice," <i>J. Neurochem.</i> , 1995; 64:936-9.			

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	H1	Stadhouders, A., <i>et al.</i> , "Mitochondrial Creatine Kinase: A Major Constituent of Pathological Inclusions Seen in Mitochondrial Myopathies," <i>PNAS</i> , 1994; 91(11):5089-93.		
	H2	Wang, T., "Synthesis and Properties of N-Acetimidoyl Derivatives of Glycine and Sarcosine," <i>JOC</i> , 1974; 39(24):3591-4.		

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